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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

NAPOLEONE FERRARA, DENIS
GOSPODAROWICZ and JEAN PLOUET
Serial No: 09/929,770
Prior Examiner: Lorraine Spector
Filed: August 14, 2001
For: ENDOTHELIAL CELL GROWTH

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FACTOR, METHODS OF ISOLATION
AND EXPRESSION

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Assistant Commissioner for Patents Washington, D.C. 20231

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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to: Box IDS, Assistant Commissioner for Patents, Washington, D.C. 20231 on November 7, 2001.

Howard M. Peters (Reg. No. 29,202)

TRANSMITTAL LETTER

Sir:

Transmitted herewith are the following documents:

- 1. Transmittal Letter (2 pgs.) in duplicate;
- 2. Transmittal of Information Disclosure Statement (2 pgs.) in duplicate; and
- 3. Postcard.

The enclosed are copies of IDS and PTO 1449 forms filed in parent application for the past 12 years. See Serial No. 08/473,276.

If additional fees are due, the Commissioner is hereby authorized to charge such fees or to credit any overpayment to Deposit Account No. 16-1331.

Respectfully submitted,

Date: November 7, 2001

Howard M. Peters (Reg. No. 29,202)

Attorney of Record

PETERS, VERNY, JONES & BIKŠA, LLP

385 Sherman Avenue, Suite 6

Palo Alto, CA 94306

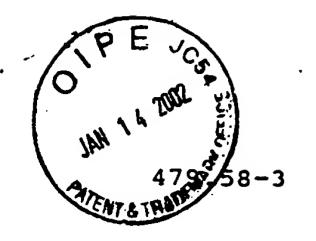
Telephone: (650) 324-1677 Facsimile: (650) 324-1678

Attorney Docket No. 479.58-6 (HMP)

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In Re A	pplication Of:	NAPOLEONE FERRARA, DENIS	S GOSPODAROWICZ and JEA	N PLOUET
	Serial No.	Filing Date	Examiner	Group Art Unit
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2.	CFR 1.97(b), pr	Disclosure Statement submitted ovided that the Information Discler 37 CFR 1.113, a Notice of prosecution in the application, a	closure Statement is filed before for Allowance under 37 CFR 1.3	e the mailing date of a
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PATENT U.C. # 89-053-3

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of

NAPOLEONE FERRARA, DENIS GOSPODAROWICZ and JEAN PLOUET

Serial No.: 360,235

Filed: June 1, 1989

For: ENDOTHELIAL CELL GROWTH

FACTOR, METHODS OF ISOLA-

TION AND EXPRESSION

Group Art Unit: 186

Examiner: S. Guest

Hon. Commissioner of Patents and Trademarks Washington, D.C. 20231

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231 on April 30, 1992.

Howard M. Peters (Reg No. 29,202)

INFORMATION DISCLOSURE STATEMENT SUPPLEMENTAL 37 C.F.R. 1.56 AND 1.97

Sir:

The citations below (copies below), which recently came to the attention of Applicants' attorney, may be material to the examination of the above-identified application and are, therefore, submitted in compliance with the duty of disclosure in 37 C.F.R. 1.56 and 1.97.

A number of these references were published after the filing date of the present or a parent patent application

The Examiner is requested to make these citations of official record in this application.

- 1. G. Beck et al., "Isolation and Characterization of A Vascular Permeability Factor from Stimulated U937 Cells," J. Leukocyte Biol., Vol. 42:5 (1987) p. 568, is an abstract describing the isolation of a vascular permeability factor (VPF) isolated from macrophage cell line U937.
- 2. J. N. Bruce et al., "Vascular permeability induced by protein product of malignant brain tumors: inhibition by dexamethasone," J. Neurosurg., Vol 67 (1987), pp. 880-884 describe an activity caused by a vascular permeability factor (VPF) found in conditioned medium from cultures of malignant human astroglial (brain) tumors. No sequence data are given for the factor.
- 3. G. R. Criscuolo et al., "Further characterization of malignant glioma-derived vascular permeability factor," J. Neurosurg., Vol. 69 (1988), pp. 254-262 describe the VPF referred to in Ref. 2 above. The factor was purified 1000 fold and postulated to have a molecular weight of 42-56 kD. No sequence data is disclosed.
- 4. D. Gospodarowicz et al., "Isolation and characterization of a vascular endothelial cell mitogen produced by pituitary-derived folliculo stellate cells," Proc. Nat. Acad. Sci., Vol. 86 (1989), pp. 7311-7315, published after the effective filing date of

the present application, describes work done by one of the inventors on the presently claimed FSdGF. An N-terminal sequence of the factor is given.

- 5. J. Plouet et al., "Isolation and characterization of a newly identified endothelial cell mitogen produced by AtT-20 cells," EMBO J., Vol. 8:12 (1989), pp. 3801-3806, published after the effective filing date of the present application describes a human vascular permeability factor, termed hVPF; the N-terminal sequence of HVPF is disclosed. The sequence was found to be similar to the sequence of guinea pig VPF.
- endothelial cell mitogen from a rat glioma-derived cell line,"

 Proc. Nat. Acad. Sci. USA, Vol. 87 (1990), pp. 1323-1327, published after the effective filing date of the present application, describes the purification of a glioma-derived vascular endothelial growth factor (GD-VEFG). An amino acid composition, but not a sequence, is disclosed. The authors state that the disclosed proteins may--or may not--be equivalent to the protein disclosed by Ferrara et al., which is presumptively the presently claimed VEGF.
- 7. G. Conn, "Amino acid and cDNA sequences of a vascular endothelial cell mitogen that is homologous to platelet-derived growth factor," Proc. Nat. Acad. Sci. USA, Vol. 87 (1990), pp. 2628-2632, published after the effective filing date of the present application, discloses the complete sequence of the GD-VEGF disclosed in Ref. 6 herein. Homology to platelet derived growth

factor (PDGF) is reported. The paper reports that the sequence of GD-VEGF is 90% similar to a recently reported VEGF sequence, and VEGF sequence (presumably derived from work on the presently claimed protein) is identical to the sequence of VPF.

- 8. D. R. Senger et al., "Purification and NH2-Terminal Amino Acid Sequence of Guinea Pig Tumor-secreted Vascular Permeability Factor," Cancer Res., Vol. 50 (1990), pp. 1774-1778, published after the effective date of the present application, disclose an N-terminal sequence of guinea pig VPF. No similarity between this sequence and previously reported sequences (in the PIR/NBRF sequence database) was found. A note added in the proof cites the work of others relating to VEGF, but no disclosure is made regarding similarity or dissimilarity between VEGF and VPF. The disclosed sequence is not identical to the sequence presently claimed, although visual inspection reveals some similarities between the two sequences.
- 9. N. Ferrara et al., "The Vascular Endothelial Growth Factor Family of Polypeptides," <u>J. Cell. Biochem.</u>, Vol. 47 (1991), pp. 211-218, published after the effective filing date of the present application, is a review of the vascular endothelial growth factors family of polypeptides. The existence of four species of VEGF polypeptides is disclosed.
- 10. C. de Vries et al., "The fms-Like Tyrosine Kinase, a Receptor for Vascular Endothelial Growth Factor," <u>Science</u>, Vol. 255 (1992), pp. 989-991, published after the effective filing date of

<u>PATENT</u>

the present application is directed to a receptor for VEGF. An introductory portion of the reference discloses the identity of VPF and VEGF sequences.

This Information Disclosure Statement under 37 C.F.R. and 1.97 is not to be construed as a representation that a search has been made, that additional information material to the examination of this application does not exist, or that any one or more of these citations constitutes prior art.

If the Examiner has any questions regarding the cited art, she is encouraged to call the undersigned attorney (collect) at (415) 421-2674.

Respectfully submitted,

Howard M. Peters (Reg. No. 29,202)

for

PHILLIPS, MOORE, LEMPIO & FINLEY 177 Post Street, Suite 800 San Francisco, California 94108

Attorneys for Applicant

HMP:cl/kw

Tel: (415) 421-2674 Fax: (415) 421-1663

Enclosures: As listed above

1P49.58-3

U.C. # 89-053-3

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the Application of

NAPOLEONE FERRARA, DENIS

MAPOLEONE FERRARA, DENIS
GOSPODAROWICZ and JEAN PLOUET

Serial No.: 360,235

Filed: June 1, 1989

For: ENDOTHELIAL CELL GROWTH

FACTOR, METHODS OF ISOLA-

TION AND EXPRESSION

Group 180

Group Art Unit: 186

Examiner: S. Guest

Hon. Commissioner of Patents and Trademarks Washington, D.C. 20231

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States postal Service as first class mail in an envelope addressed to Commissioner of Patents and Trademarks, Washington, D.C. 20231 on June 18, 1991.

Howard M. Peters (Reg. No. 29,202)

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. 1.56 AND 1.97

Sir:

The citations below, copies attached, may be material to the examination of the above-identified application and are, therefore, submitted in compliance with the duty of disclosure in 37 C.F.R. 1.56 and 1.97.

The Examiner is requested to make these citations of official record in this application.

1. D.T. Connolly et al., U.S. Patent 5,008,196, issued April

16, 1991, class 435/240.2.

- 2. California Biotechnology, Inc., International Publ. No. WO 91/02058, published 21 February 1991, PCT/US90/04227, filed 27 July 1990.
- 3. Edmund Tischer et al., "Vascular Endothelial Growth Factor: A New Member of the Platelet-Derived Growth Factor Gen Family," <u>Biochemical & Biophysical Research Communications</u>, Vol. 165 (3), pp. 1198-1206.

This Information Disclosure Statement under 37 C.F.R. and 1.97 is not to be construed as a representation that a search has been made, that additional information material to any examination of this application does not exist, or that anyone or more of these citations constitutes prior act.

If the Examiner has any questions regarding the cited Art, she is encouraged to call the undersigned attorney (collect) at (415) 421-2674.

Respectfully submitted,

Howard M. Peters (Reg. No. 29,202)

for

PHILLIPS, MOORE, LEMPIO & FINLEY 177 Post Street, Ste. 800 San Francisco, CA 94108

Attorneys for Applicants

HMP:cl (415) 421-2674

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<u>PATENT</u> U.C. # 89-053-3

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

re the Application of

NAPOLEONE FERRARA, DENIS GOSPODAROWICZ and JEAN PLOUET

Serial No.: 360,235

Filed: June 1, 1989

FOR: ENDOTHELIAL CELL GROWTH FACTOR, METHODS OF ISOLATION AND EXPRESSION

Hon. Commissioner of Patents and Trademarks Washington, D.C. 20231 Group 180

Group Art Unit: 186

Examiner: S. Guest

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States postal Service as first class mail in an envelope addressed to Commissioner of Patents and Trademarks, Washington, D.C. 20231 on October 25, 1990.

Howard M. Peters (Reg. No. 29,202)

INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. 1.56 AND 1.97 Sir:

The citations below, copies attached, may be material to the examination of the above-identified application and are, therefore, submitted in compliance with the duty of disclosure in 37 C.F.R. 1.56 and 1.97.

The Examiner is requested to make these citations of official record in this application.

- H.F. Dvorak, et al., U.S. Patent 4,456,550, issued June
 1984, class 260/112R.
- 2. European Patent Application Publication 0370,989, published May 30, 1990, class C12N 15/12.
 - 3. H.F. Dvorak, et al. WO 84/02135, PCT, published June 7,

1984, Int. Class C07G 7/00.

- 4. D.W. Leung, et al., "Vascular Endothelial Growth Factor Is a Secreted Angiogenic Mitogen", Science, Vol. 246, p. 1306 (December 8, 1989).
- 5. P.J. Keck, et al., "Vascular Permeability Factor, an Endothelial Cell Mitogen Related to PDGF", <u>Science</u>, Vol. 246, p. 1309, (December 8, 1989).
- 6. G.E. Lemke, et al., "Identification and Purification of Glial Growth Factor¹", <u>Journal of Neuroscience</u>, Vol. 4, No. 1, p. 75 (January 1984).
- 7. N. Ferrara, et al., "Pituitary Follicular Cells Secrete a Novel Heparin-Binding Growth Factor Specific for Vascular Endothelial Cells", <u>Biochemical and Biophysical Research Communications</u> Vol. 161, No. 2, p. 851, (June 15, 1989).
- 8. D. Gospodarowicz, et al., "Isolation and Characterization of a Vascular Endothelial Cell Mitogen Produced by Pituitary Derived Folliculo Stellate Cells", <u>Biochemistry</u>, Vol. 86 p. 882 (1989).
- 9. D. Gospodarowicz, et al., "Pituitary Follicular Cells Secrete Both Vascular Endothelial Cell Growth Factor and Follistatin" as submitted earlier to related U.S. Patent Application Serial No. 07/346,169 filed May 2, 1990.
- 10. N. Ling, et al., "Isolation and partial characterization of a M_r 32,000 protein with inhibin activity from porcine follicular fluid", <u>Biochemistry</u>, Vol. 82, p. 7217 (November 1985).
- 11. N. Ueno, et al., "Isolation and partial characterization of follistatin: A single-chain M_r 35,000 monomeric protein that inhibits the release of follicle-stimulating hormone", Biochemistry, Vol. 84, p. 8282 (December 1987).

If the Examiner has any questions regarding the cited Art, she is encouraged to call the undersigned attorney (collect) at (415) 421-2674.

Respectfully submitted,

Howard M. Peters (Reg. No. 29,202)

for

PHILLIPS, MOORE, LEMPIO & FINLEY

177 Post Street, Ste. 800 San Francisco, CA 94108

(415) 421-2674

Attorneys for Applicant

HMP:cal A:479-58.3/disclosure

SERIAL NO. PTO-1449 (Modified) ATTY. DOCKET NO. OF PATENTS AND PUBLICATIONS FOR 479.58-3 O/ 360,235 APPLICANT'S INFORMATION DISCLOSURE **APPLICANT** N. FERRARA et al. STATEMENT (Use several sheets if necessary) FILING DATE GROUP 186 6/1/89 REFERENCE DESIGNATION U.S. PATENT DOCUMENTS EXAMER FLING DATE MIM DOCUMENT NUMBER DATE NAME auss SEALORE F APPROPRIATE 0 0 8 19 6 4/16/91 Connolly et al 435/240.2 **A8** KC AD Æ AG AH N FOREIGN PATENT DOCUMENTS TRANSLATION DOCUMENT NUMBER DATE COUNTRY SUBCLUSS auss YES NO 2 0 5 8 published 21/2/91 Patient Cooperation Treaty W 10 **OTHER** ART (Including Author, Title, Date, Pertinent Pages, Etc.) Edmund Tischer et al., 'Vascular Endothelial Growth Factor: A New Member of the Platelet-Derived Growth Factor Gene Family," AR Biochemical & Biophysical Research Communications, Vol. 165(3), pp. 1198-1206. AS AT EXAMINER DATE CONSIDERED

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